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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/778,168	WRIGHT ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-19,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-19,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 13 January 2005 in which claim 1 was amended and claim 20 was canceled. The amendments have been thoroughly reviewed and entered.

The previous objections and rejections in the Office Action dated 23 August 2004 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection, necessitated by amendment, are discussed.

Claims 1, 3-19 and 21-22 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 3-5, 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996) in view of Fauser et al (BioTechniques, 1997, 22(5): 964-968).

Regarding Claim 1, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal

nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. β+ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54). While the method steps do not require isothermal amplification, Caskey et al teach the amplification via hybridization and primer extension (as claimed) wherein the extension utilizes DNA polymerase (Klenow) at a single temperature e.g. 37° C for 30 minutes (Column 8, lines 17-21).

While Caskey et al teaches a diagnostic nucleotide 5 nucleotides from the 3' terminal, they do not teach 2 to 4 nucleotides from the 3' end. However, diagnostic nucleotides 2 to 4 nucleotides from the 3' nucleotide were known in the art as taught by Fauser et al (page 966, Fable 1). Fauser et al further teach these primers improve allele-specificity (page 965, lines 1-4). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to re-position the diagnostic nucleotide of Caskey et al to a position between 2 to 4 bases of the 3' nucleotide as taught by Caskey et al for the expected benefit of improved allele specificity as taught by Fauser et al (page 965, lines 1-4). One of ordinary skill in the art would have been further motivated to re-position the diagnostic nucleotide using routine experimentation to optimize allele-specific primers.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 3, Caskey et al teach the method using multiple detector primers, each comprising different diagnostic nucleotides (e.g. M vs S or Z, Example 4).

Regarding Claim 4, Caskey et al teach the method wherein the two primers are used to identify which of two possible SNP is present (e.g. M vs S or Z, Example 4).

Regarding Claim 5, Caskey et al teach the method wherein four detector primers are used (e.g. M (1) vs Z (2) and M(3) vs S(4), Example 4).

Regarding Claim 7, Caskey et al teach the method wherein detector primers have a non-diagnostic mismatch (Column 5, lines 20-46).

Regarding Claim 8, Caskey et al teach the method wherein the non-diagnostic nucleotide is within 15 nucleotides of the detector nucleotide i.e. the primers are preferably 12-16 (Column 4, lines 39-40). Hence, the non-diagnostic nucleotide is within 15 as claimed.

Regarding Claims 9-10, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. $\beta+$ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54).

Caskey et al further teach detector primers having non-diagnostic mismatch nucleotides whereby the more perfectly matched primer will be favored in the amplification reaction (Column 5, lines 20-46). Caskey et al also teach the primers are preferably 12-16 (Column 4, lines 39-40) and they illustrate diagnostic nucleotides positioned 5 bases from the terminal nucleotide (Examples 3-4). They do not specifically teach the non-diagnostic nucleotide 5 nucleotides from or adjacent to the diagnostic nucleotide. However, the addition of a non-diagnostic nucleotide (as they clearly suggest) to their exemplified 12 nucleotide primers would position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide. Hence, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add a non-diagnostic nucleotide to the diagnostic primer of Caskey and to position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide based on the available nucleotide positions within the 12 nucleotide primers exemplified by Caskey et al.

Regarding Claim 11, Caskey et al teach the method wherein the detector primer is 15-36 nucleotides (Column 4, lines 37-41).

Regarding Claim 12, Caskey et al teach the method wherein the detector primer is 18-24 nucleotides (Column 4, lines 37-41).

Regarding Claim 13, Caskey et al teach the method wherein the amplification is nucleic acid based amplification (Column 7, lines 31-50).

Regarding Claim 14, Caskey et al teach the method wherein the detector primer is 12-50 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 15, Caskey et al teach the method wherein the detector primer is 12-24 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 16, Caskey et al teach the method wherein the detector primer is 12-19 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 17, Caskey et al teach the method wherein the SNP is detected by means of a label attached to the primer (Column 6, lines 16-35).

4. Claims 6 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996) in view of Fauser et al (BioTechniques, 1997, 22(5): 964-968) as applied to Claim 1 above and further in view of Whitcombe et al (U.S. Patent No. 6,326,145, filed 25 November 1998).

Regarding Claims 6 and 18-22, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the

efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. $\beta+$ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54).

Caskey et al also teach primers labeled using art recognized techniques (Column 6, lines 16-35) but they do not teach tailed primers, primers detectable upon extension, primers labeled with donor/quencher dyes, quantitatively detected and displaced by an upstream primer.

However, these elements were well known in the art at the time the claimed invention was made as taught by Whitcombe et al (Column 4, lines 31-65) wherein binding results in abolished signal (Column 4, lines 49-53). Whitcombe et al further teach their method is useful for strand displacement (Column 5, lines 57-59) and especially quantitative allele discrimination (Column 6, lines 33-43 and Column 10, line 60-Column 11, line 17).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the tailed primers having donor/quencher dye attached as taught by Whitcombe et al to the allele-specific primers of Caskey et al for the expected benefit of providing quantitative analysis of clinically important nucleic acids e.g. HIV nucleic acids as taught by Whitcombe et al (Column 6, lines 33-43).

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Art Unit: 1634
March 30, 2005